

APPENDIX A

CLAIMS:

1. (Twice Amended) A method of providing a polypeptide preparation having a ~~reduced~~ content of undesired enzymatic side activities at such a level that they do not restrict the applicability of said polypeptide preparation for its intended purpose, the method comprising the steps of:
 - (i) providing a medium having a pH of 2.0 or higher that comprises at least one desired polypeptide having an enzymatic activity and in addition ~~hereto~~ at least one undesired enzymatic side activity, and
 - (ii) subjecting said medium to a pH of less than 2.0 for a period of time that is sufficient to at least partially inactivate said ~~the~~ at least one undesired enzymatic side activity.
2. (Amended) A method according to claim 1, wherein at least 75% of the enzymatic activity of said ~~the~~ at least one desired polypeptide is retained after subjecting ~~the~~ said medium having a pH of 2.0 or more to a pH of less than 2.0.
3. (Amended) A method of claim 2, wherein at least 85% of the enzymatic activity of ~~the~~ said at least one desired polypeptide is retained.
4. (Twice Amended) A method according to claim 1, wherein at least 50% of ~~the~~ activity of ~~the~~ said at least one undesired enzymatic activity is inactivated.
5. (Amended) A method according to claim 4, wherein at least 90% of ~~the~~ activity of ~~the~~ said at least one undesired enzymatic activity is inactivated.
6. (Amended) A method according to claim 1, wherein the medium having a pH of 2.0 or higher is a medium derived from the cultivation of an organism that during its cultivation produces ~~the~~ said at least one desired polypeptide and ~~the~~ said at least one undesired enzymatic side activity.

7. A method according to claim 1, wherein the at least one desired polypeptide is selected from the group consisting of an enzyme, an antibody, an antigen and a pharmaceutically active polypeptide.

8. (Amended) A method according to claim 1, wherein ~~the said~~ at least one undesired enzymatic side activity is selected from the group consisting of glucoamylase activity, starch degrading enzyme activity, protease activity, peptidase activity, phosphatase activity, lipase activity, cellulase activity, lactase activity and hemicellulase activity.

9. A method according to claim 1, wherein the medium having a pH of 2.0 or higher is derived from the cultivation of an organism that is selected from the group consisting of an animal species, a plant species, a bacterial species, a yeast species and a species of filamentous fungi.

10. (Amended) A method according to claim 9, wherein the bacterial species is selected from the group consisting of a gram negative bacterial species ~~including *E. coli*~~ and a gram positive species ~~including a *Bacillus* species~~.

11. (Amended) A method according to claim 9, where the yeast species is selected from the group consisting of *Saccharomyces cerevisiae*, a methylotrophic yeast species ~~including *Pichia pastoris*~~ and a *Klyuveromyces* species ~~including *Klyuveromyces lactis*~~.

12. A method according to claim 9, wherein the species of filamentous fungi is selected from the group consisting of an *Aspergillus* species, a *Cryphonectria* species, a *Fusarium* species, a *Rhizomuor* species and a *Trichoderma* species.

13. A method according to claim 1, wherein the medium having a pH of 2.0 or higher is subjected to a pH in the range of 1.0 to 1.99.

14. A method according to claim 13, wherein the pH is in the range of 1.5 to 1.99.

15. A method according to claim 14, wherein the pH is in the range of 1.7 to 1.99.
16. A method according to claim 15, wherein the pH is about 1.8.
17. A method according to claim 13, wherein the pH in the range of 1.0 to 1.99 is provided by adding an inorganic or an organic acid.
18. A method according to claim 1, wherein the medium having a pH of 2.0 or higher is subjected to a pH of less than 2.0 for a period of time that is in the range of 0.1 minutes to 48 hours.
19. (Amended) A method according to claim 1, wherein ~~the~~ said at least one desired polypeptide has aspartic protease activity.
20. (Amended) A method according to claim 19, wherein the medium having a pH of 2.0 or higher is a medium derived from the cultivation of a microorganism that during the cultivation produces ~~the~~ an aspartic protease and ~~the~~ said at least one undesired enzymatic side activity.
21. (Amended) A method according to claim 20, wherein the medium is derived from the cultivation of a microorganism that naturally produces the aspartic protease or from the cultivation of a recombinant microorganism that has an inserted gene expressing the aspartic protease.
22. A method according to claim 21, wherein the microorganism is selected from the group consisting of a bacterial species, a yeast species and a species of filamentous fungi.
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23. (Amended) A method according to claim 22, wherein the aspartic protease is expressed as a fusion protein having, in addition to the aspartic protease activity, at least one undesired enzymatic side activity.

24. (Amended) A method according to claim 23, wherein ~~the said~~ at least one enzymatic side activity is starch degrading enzyme activity ~~including an activity selected from the group consisting of amylase activity and glucoamylase activity.~~

25. A method according to claim 20, wherein the microorganism is one that naturally produces at least one enzymatic side activity.

26. (Amended) A method according to claim 25, wherein ~~the said~~ at least one undesired enzymatic side activity is selected from the group consisting of glucoamylase activity, lactase activity, starch degrading enzyme activity, protease activity, peptidase activity, phosphatase activity, lipase activity, cellulase activity and ~~hemicellulase~~ hemicellulase activity.

27. (Twice Amended) A method according to claim 19, wherein the aspartic protease is derived from the group consisting of an animal aspartic protease ~~including a mammalian aspartic protease~~, a plant aspartic protease and a microbial aspartic protease.

28. (Amended) A method according to claim ~~27~~38, wherein the mammalian aspartic protease is selected from the group consisting of pro-chymosin, chymosin, pepsinogen and pepsin.

29. (Amended) A method according to claim 28, wherein the aspartic protease is derived from a mammalian species selected from the group consisting of a ruminant species, a *Camrnelidae* species ~~including Camelus dromedarius~~, a porcine species, an *Equidae* species and a primate species.

30. A method according to claim 29, wherein the ruminant species is selected from the group consisting of a bovine species, an ovine species, a caprine species, a deer species, a buffalo species, an antelope species and a giraffe species.

31. (Amended) A method according to any of claims ~~27, 28-30~~ or 38, wherein the mammalian derived aspartic protease is a protease naturally produced in a mammalian species.

32. (Amended) A method according to claim 27, wherein the aspartic protease is derived from a naturally produced aspartic protease by the addition ~~of~~ or deletion of one or more amino acids or substitution of one or more amino acids ~~herein~~ therein.

33. (Withdrawn) A milk clotting composition comprising a preparation of an aspartic protease, provided by the method of any of claims 1-32, said composition essentially not having undesired enzymatic side activities.

34. (Withdrawn) A composition according to claim 33 essentially not having an undesired enzymatic side activity selected from the group consisting of glucoamylase activity, lactase activity, starch degrading enzyme activity, protease activity, peptidase activity, phosphatase activity, lipase activity, cellulase activity and hemicellulase activity.

35. (New) A method according to claim 10, wherein the bacterial species is selected from *E. coli* and *Bacillus*.

36. (New) A method according to claim 9, wherein the yeast species is selected from *Pichia pastoris* and *Kluyveromyces lactis*.

37. (New) A method according to claim 24, wherein said starch degrading enzyme activity is selected from amylase activity and glucoamylase activity.

38. (New) A method according to claim 27, wherein said animal aspartic protease is a mammalian aspartic protease.

39. (New) A method according to claim 29, wherein the *Camelidae* species is *Camelus dromedarius*.